RESEARCH AND TRAINING DETAILS

- Number of Faculty: 7
- Number of Joint Appointment Faculty: 2
- Number of Research Fellows: 4
- Number of Research Students: 12
- Number of Support Personnel: 22
- Direct Annual Grant Support: $3,596,379
- Peer Reviewed Publications: 16

CLINICAL ACTIVITIES AND TRAINING

- Number of Clinical Staff: 1

Significant Accomplishments

Genetic and Environmental Influences on Asthma Development Systems

Gurjit Khurana Hershey, MD, PhD, is the principal investigator of an NIH-funded Asthma and Allergic Diseases Cooperative Research Center and serves on its steering committee. The Cincinnati Center is one of only 11 such centers in the United States. The Center has identified several epithelial genes with previously unrecognized roles in asthma. Further analyses suggest that some of these genes are specific to one epithelial surface and are associated with one allergic disease, while others are common to multiple surfaces and disorders. By identifying epithelial genes and pathways that predispose individuals to allergic disorders, we are advancing the search for novel, targeted therapeutics. Furthermore, integration of data will provide novel insights into a key question in allergy - What are the mechanisms underlying tissue specific disease manifestations of allergic inflammation? We have made significant progress and several manuscripts have been published, with more in preparation.

Cincinnati Children’s Studies Inner City Asthma

Cincinnati Children’s is one of nine contracted clinical research sites funded to study the treatment and prevention of asthma in inner-city asthma populations by conducting several clinical trials and mechanistic studies in order to understand the immunopathogenesis of the disease and to evaluate and develop effective interventions tailored to inner-city populations. Khurana Hershey is the PI of the Inner City Asthma Consortium (ICAC) at the Cincinnati site. The study’s goals are to improve asthma control, to improve asthma phenotyping
using biomarkers, to develop allergen immunotherapy approaches for cockroach allergy, to conduct further studies of asthma in the inner-city, and to develop, validate and implement the basic science methodology to support these objectives. ICAC is the nation’s largest effort to study asthma in the inner city. To date, Cincinnati Children’s has participated in three ICAC clinical trial studies and look forward to participating in many more in the years to come.

Ohio Children’s Hospitals Collaborate to Analyze Asthma Hospitalizations
Khurana Hershey has been working with five other children’s hospitals in Ohio to develop the Ohio Pediatric Asthma Repository (OPAR) to identify practices that result in the best health outcomes for children with asthma. OPAR is being used to conduct observational, comparative effectiveness, and intervention studies for pediatric asthma. To date OPAR has enrolled 2,456 participants statewide.

Research Highlights

Gurjit Khurana Hershey, MD, PhD
- Dr. Gurjit Khurana Hershey was nominated and elected to serve as a member of the American Society for Clinical Investigation (ASCI). The ASCI established in 1908, is one of the nation’s oldest and most respected medical honor societies. The ASCI represents active physician-scientists who are at the bedside, at the research bench, and at the blackboard. Many of its senior members are widely recognized leaders in academic medicine.
- Dr. Gurjit K Khurana Hershey was recently elected into the University of Cincinnati’s Fellows of the Graduate School. The Fellows of the Graduate School is an organization that recognizes distinguished researchers and scholars from throughout the University of Cincinnati. Fellows are generally among the most experienced and accomplished graduate-student mentors at the University. Along with having an important role in graduate education and research, the Fellows are also called upon to provide regular feedback on new initiatives and to review research proposals at all levels of the University.
- Dr. Gurjit K. Khurana Hershey has been selected as a fellow in the Association of Medical School Pediatric Department Chairs’ (AMSPDC) Pediatric Leadership Development Program. The PLDP fellowship program aims to help develop the next generation of pediatric chairs in North America, ensuring that they will be well poised to lead our profession through the rapidly changing environment of academic medicine and health care in general.

Melinda Butsch Kovacic, MPH, PhD
- Dr. Melinda Butsch Kovacic and colleagues were awarded a grant to fund a pilot study, “Resilient Kids”, using surveys and biomarkers to assess stress and resiliency coping in three distinct yet vulnerable populations (Appalachian, Latino, and African American) in partnership with the community.
- Dr. Melinda Butsch Kovacic partnered with the College of Allied Health to submit a grant to Aetna to support “Healthy Fun Fridays” at the Findlay Street Neighborhood House.
- Dr. Melinda Butsch Kovacic was accepted to the Cincinnati Regional Chamber of Commerce Leadership Action Class Program and jointed the Cincinnati Children’s Research Participant Advisory Council.

Tesfaye B Mersha, PhD
- Dr. Tesfaye Mersha was accepted to participate in the PRIDE (Programs to Increase Diversity Among Individuals Engaged in Health-Related Research) Program in Cardiovascular Genetic Epidemiology. The primary objective of the program funded by the National Heart, Lung, and Blood Institute (NHLBI) is to provide all-expense-paid training and mentoring in genetic epidemiology with a focus on Cardiovascular and other Heart, Lung, Blood, and Sleep Disorders to junior faculty and scientists from minority groups.
that are under-represented in biomedical research. This program prepares the participant to competently and effectively develop independent research programs.

**Significant Publications**


In children with allergic asthma, diesel exhaust particles (DEP) exposure was found to be associated with more frequent asthma symptoms and increased IL-17A blood levels. Similarly, DEP exposure worsened the allergic asthma phenotype in an experimental asthma model, resulting in increased airway hyperresponsiveness, allergen sensitization, BALF Th2 and Th17 cytokines levels, and pulmonary eosinophilia compared with house dust mite alone. Exposure to DEPs alone induced a Th17 response associated with neutrophilia but did not result in airway hyperresponsiveness, eosinophilia, Th2 cytokines, or mucous production. IL-17A neutralization alleviated DEP-induced airway hyperresponsiveness in mice, indicating IL-17A might be a useful potential therapeutic strategy to counteract the asthma-promoting effects of traffic-related air pollution, especially in highly exposed patients with severe allergic asthma.


IL-13 is a central mediator of allergic inflammation and asthma. IL-13 mediates its effects through receptors, including IL-4 receptor alpha, IL-13 receptor alpha 1, and IL-13 receptor alpha 2 (IL-13Ra2). Some IL-13 antagonists have already been tested in clinical trials. Most preclinical studies for these IL-13 antagonists were done in mice. Our data clearly demonstrate that human and murine IL-13 biology are markedly different, specifically with regards to IL-13Ra2. IL-13Ra2 binds IL-13 with high affinity and can modulate IL-13 responses. There are soluble and membrane forms of IL-13Ra2 generated by alternative splicing in mice, but human subjects express only the membrane form of IL-13Ra2. Mice have nanogram quantities of soluble IL-13Ra2 in their serum while humans lack serum soluble IL-13Ra2. The serum concentration of soluble IL-13Ra2 is ~10-fold greater than that of IL-13 on a molar basis, which is sufficiently high to inhibit IL-13 signaling in mice. Our early studies support a limited role for soluble form of IL-13Ra2 in humans, highlighting the potential importance of membrane form of IL-13Ra2 in human immunity. Our recent studies demonstrate that membrane form of IL-13Ra2 has a distinct role in the lung and contributes to the development of allergic inflammation. The studies on the roles of membrane versus soluble IL-13Ra2 will enable the design of the most effective targeted therapies.


Despite the important role for epidermal growth factor (EGF) in epithelial homeostasis and wound healing, it has not been investigated in atopic dermatitis (AD). We used AD animal models to explore the role of EGF in AD. In an acute AD model, skin transepidermal water loss was significantly attenuated in EGF-treated mice. EGF treatment did not alter expression of skin barrier junction proteins or antimicrobial peptides in the AD model. However, EGF treatment attenuated allergen-induced expression of IL-17A, CXCL1, and CXCL2 and neutrophil accumulation in AD skin following cutaneous allergen exposure. IL-17A production was decreased in the in vitro restimulated skin-draining lymph node cells from the EGF-treated mice. Similarly, IL-17A was
increased in waved-2 mice skin following allergen exposure. Whereas IL-6 and IL-1β expression was attenuated in the skin of EGF-treated mice, EGF treatment also suppressed allergen-induced IL-6 production by keratinocytes. Given the central role of IL-6 in priming Th17 differentiation in the skin, this effect of EGF on keratinocytes may contribute to the protective roles for EGFR in AD pathogenesis. In conclusion, our study provides evidence for a previously unrecognized protective role for EGF in AD and a new role for EGF in modulating IL-17 responses in the skin.

Division Publications

14. Wei Q, Sha Y, Bhattacharya A, Abdel Fattah E, Bonilla D, Jyothula SS, Pandit L, Khurana Hershey GK, Eissa NT. Regulation of IL-4 receptor signaling by STUB1 in lung inflammation. Am J Respir Crit Care


Faculty, Staff, and Trainees

Faculty Members

Gurjit Khurana Hershey, MD, PhD. Professor
  Leadership Division Director; Kindervelt Endowed Chair; Director, Medical Scientist Training Program; Co-Director, Office of Pediatric Clinical Fellowships
  Research Interests Integrating clinical, translational, and basic research to identify genetic and environmental factors that promote asthma prevention, management, and treatment.

Jocelyn Biagini Myers, PhD, Assistant Professor
  Research Interests Role of genetics in secondhand smoke-related pediatric asthma.

Melinda Butsch Kovacic, MPH, PhD, Associate Professor
  Leadership Secretary/President, Cincinnati Children's Women's Faculty Association
  Research Interests Using classical and molecular epidemiological approaches to evaluate environmental, infectious, genetic, and socioeconomic causes of chronic disease with current focuses on asthma and Fanconi anemia.

Weiguo Chen, MD, PhD, Assistant Professor
  Research Interests Mechanisms underlying airway hyperresponsiveness, inflammation and remodeling of allergic asthma.

Hong Ji, PhD, Assistant Professor
  Leadership Director, Pyrosequencing Core
  Research Interests Epigenetic plasticity of development and disease; asthma epigenetics; environmental epigenetics; genome-wide and locus specific DNA methylation analysis; epigenetic regulation of gene expression

Tesfaye Mersha, PhD, Assistant Professor
  Research Interests Integrating and using genomics, statistical genetics, biological profiling and pathway methods to elucidate the genetic architecture of complex diseases of public significance, including asthma.

Umasundari Sivaprasad, PhD, Assistant Professor
  Research Interests Allergic inflammation; atopic dermatitis; asthma; development of anti-inflammatory therapies

Trainees
  - Eric Brandt, PhD, PGY12, Institut Pasteur de Lille, France
  - Lili Ding, PhD, PY3, University of Cincinnati
Division Collaboration

Asthma and Allergic Diseases Cooperative Research Center funded by the NIH. (Gurjit K. Khurana Hershey, MD, PhD; Melinda Butsch Kovacic MPH, PhD; Umasundari Sivaprasad, PhD)

Allergy and Immunology » Pablo Abonia, MD, Simon Hogan, PhD, and Marc Rothenberg, MD, PhD
Human Genetics » Lisa J. Martin, PhD

The Division of Asthma Research partners with the Pulmonary Asthma Center to form the Cincinnati Children's Asthma Program to improve the health of children with asthma by integrating the evidence-based clinical care with innovative research that will lead to personalized asthma therapy for children living in the Greater Cincinnati area. Drs. Gurjit Khurana Hershey and Carolyn Kercsmar participate in an NIH-funded study entitled "Inner City Asthma Consortium" aimed at preventing asthma in inner-city children. (Gurjit K. Khurana Hershey, MD, PhD)

Pulmonary Medicine » Carolyn Kercsmar, MD

Impact of Early Life Diesel Exposure on Immune Patterning and Lung Structure/Function grant. (Gurjit K. Khurana Hershey, MD, PhD)

Section of Neonatology, Perinatal and Pulmonary Biology » Tim LeCras, PhD

Ohio Pediatric Asthma Repository. (Gurjit K. Khurana Hershey, MD, PhD)
Pulmonary Medicine » Theresa Guilbert, MD and Carolyn Kercsmar, MD
Hospital Medicine » Jeffrey Simmons, MD
Human Genetics » Lisa J. Martin, PhD

HPV Replication and Transformation in FA Squamous Cell Carcinomas; HPV Prevalence Studies in Fanconi Anemia Population. (Melinda Butsch Kovacic, MPH, PhD)
Cancer and Blood Diseases Institute » Susanne Wells, PhD, Stella Davies, PhD, Kasiangi Myers, MD, and Parinda Mehta, MD
Pulmonary Medicine » Daniel Grossoehme, Dmin
Human Genetics » Lisa J. Martin, PhD

Role of Serpinb3a in goblet cell hyperplasia. (Umasundari Sivaprasad, PhD)
Section of Neonatology, Perinatal and Pulmonary Biology » Jeffrey Whitsett, MD, Susan Wert, PhD, and Timothy LeCras, PhD

Epigenetic regulation of dendritic cell differentiation. (Hong Ji, PhD)
Rheumatology » Matt Weirauch, PhD

Transcriptional regulation of IL-17 induced genes in the nasal epithelium. (Gurjit K. Khurana Hershey, MD, PhD; Umasundari Sivaprasad, PhD)
Immunobiology » Ian Lewkowich, PhD
Epigenetic Analysis of Individuals with Asthma and Non-Asthmatic Controls. (Melinda Butsch Kovacic, MPH, PhD)

**Biostatistics and Epidemiology** » Patrick Ryan, PhD

Effects of environmental exposures on systemic oxidative stress levels and allergic disease risk and severity in individuals with asthma and allergies. (Melinda Butsch Kovacic, MPH, PhD)

**Biostatistics and Epidemiology** » Patrick Ryan, PhD and Nanhua Zhang, PhD

**Human Genetics** » Lisa J. Martin, PhD

Immunologic Basis for Adverse Health Effects of Particulate Exposure on Childhood Asthma. (Gurjit K. Khurana Hershey, MD, PhD; Jocelyn Biagini Myers, PhD)

**Section of Neonatology, Perinatal and Pulmonary Biology** » Timothy LeCras, PhD

**Biostatistics and Epidemiology** » Patrick Ryan, PhD

Nasal Epithelial Cell Study. (Gurjit K. Khurana Hershey, MD, PhD)

**Human Genetics** » Lisa J. Martin, PhD

Human Dendritic Cell Differentiation project. (Hong Ji, PhD)

**Immunobiology** » Edith Janssen, PhD

CoreChange Project & Findlay Street Neighborhood House Community Project. (Melinda Butsch Kovacic, MPH, PhD)

**Pediatric General and Thoracic Surgery** » Victor Garcia, MD

Personalized Multimedia Discharge Instructions Study. (Melinda Butsch Kovacic, MPH, PhD)

**Emergency Medicine** » Lisa Vaugh, PhD

**Biostatistics and Epidemiology** » Nanhua Zhang, PhD

**Pulmonary Medicine** » Carolyn Kercsmar, MD

Characterizing the mechanistic basis for the protective function of Stard7 in the lungs. (Gurjit K. Khurana Hershey, MD, PhD)

**Section of Neonatology, Perinatal and Pulmonary Biology** » Timothy Weaver, PhD

Ancestry informative markers development for morphine related pain medication. (Tesfaye Mersha, PhD)

**Anesthesiology** » Senthil Sadhasivam, MD, MPH

Admixture mapping in asthmatic African American children. (Tesfaye Mersha, PhD)

**Human Genetics** » Lisa J. Martin, PhD

Severe asthmatics and rare variants association in admixed asthmatic children. (Tesfaye Mersha, PhD)

**Pulmonary Medicine** » Carolyn Kercsmar, MD

Rare variants in admixed asthmatic children. (Tesfaye Mersha, PhD)

**Biostatistics and Epidemiology** » Lili Ding, PhD and Mekibib Altaye, PhD
Resilient Kids Study. (Melinda Butsch Kovacic, MPH, PhD)

Emergency Medicine » Lisa Vaughn, PhD

Cincinnati Childhood Asthma and Air Pollution Study. (Gurjit K. Khurana Hershey, MD, PhD)

Biostatistics and Epidemiology » Patrick Ryan, PhD

Unraveling relationships of TRAP, genes and development on lung and brain outcomes. (Gurjit K. Khurana Hershey, MD, PhD)

Biostatistics and Epidemiology » Patrick Ryan, PhD

General and Community Pediatrics » Kim Yolton, PhD

Section of Neonatology, Perinatal and Pulmonary Biology » Timothy LeCras, PhD, Charles Vorhees, PhD, and Timothy Weaver, PhD

Immunologic Basis for Adverse Health Effects of Particulate Exposure on Childhood Asthma. (Gurjit K. Khurana Hershey, MD, PhD; Jocelyn Biagini Myers, PhD)

Biostatistics and Epidemiology » Patrick Ryan, PhD

Human Genetics » Lisa J. Martin, PhD

Section of Neonatology, Perinatal and Pulmonary Biology » Timothy LeCras, PhD

Immunobiology Graduate Program. (Gurjit K. Khurana Hershey, MD, PhD)

Immunobiology » David Hildeman, PhD

Role of Vanin-1 in Difficult-to-treat asthma. (Gurjit K. Khurana Hershey, MD, PhD)

Human Genetics » Lisa J. Martin, PhD

Rheumatology » Matt Weirauch, PhD

Asthma Home Visits Study. (Gurjit K. Khurana Hershey, MD, PhD)

General and Community Pediatrics » Nicholas Newman, DO, MS, FAAP

Placenta Growth Factor links the Th2 response and the Leukotriene pathway and augment airway hyper-responsiveness. (Gurjit K. Khurana Hershey, MD, PhD)

Experimental Hematology » Punam Malik, MD

Birth Cohort Study. (Gurjit K. Khurana Hershey, MD, PhD)

Perinatal Institute » Louis Muglia, MD, PhD

Grants, Contracts, and Industry Agreements

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HERSHEY, G
Epithelial Genes in Allergic Inflammation
National Institutes of Health
U19 AI 070235 09/01/11-08/30/16 $1,309,226

Rothenberg, M Project 2 $238,496
Martin, L AADCRC Core $87,790

Inner City Asthma Center
National Institutes of Health(University of Wisconsin-Madison)
HHSN272200900052C 10/01/11-09/30/14 $513,040

Ohio Children's Hospitals Asthma Task Force
Ohio Department of Jobs and Family Services(Nationwide Children's Hospital)
G-1213-07-0561 07/01/12-06/30/14 $846,585

HERSHEY, G / LECRAS T
Impact of Early Life Diesel Exposure on Immune Patterning and Lung Structure/Function
National Institutes of Health
R01 HL 097135 09/01/09-07/31/14 $305,215

JI, HONG
DNA Methylation in Children Hospitalized with Asthma Exacerbation
National Institutes of Health
R21 AI 101375 08/01/12-07/31/14 $117,500

Impact of Diesel Exposure on the Methylome of Human Induced Pluripotent Stem Cells Derived From Airway Epithelial Cells
National Institutes of Health(University of Texas Health Science Center)
U19 AI 070412 04/01/13-06/30/14 $50,000

MERSHA, T
Admixture Mapping in African American Asthmatic Children
National Institutes of Health
K01 HL 103165 07/14/10-05/31/15 $118,974

MINTZ-COLE, R
Regulation of Foxp3 Expression by DNA Methylation in Mold-Induced Asthma
National Institutes of Health
F30 HL 103087 07/01/10-06/30/14 $43,032

ZHANG, Z
Molecular Epidemiology in Children's Environmental Health Training Program
National Institutes of Health(University of Cincinnati)
T32 ES 010957 09/01/12-06/30/14 $39,850

Current Year Direct $3,596,379
Total $3,596,379